A Convenient Synthesis of (2-Styrylchromon-8-yl)acetic Acids

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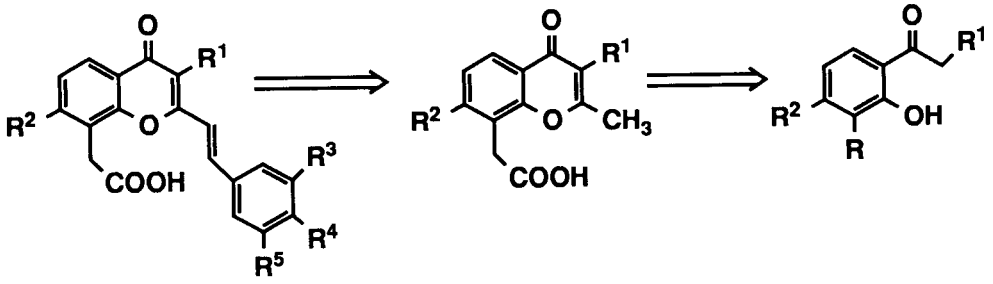
Received March 12, 1991

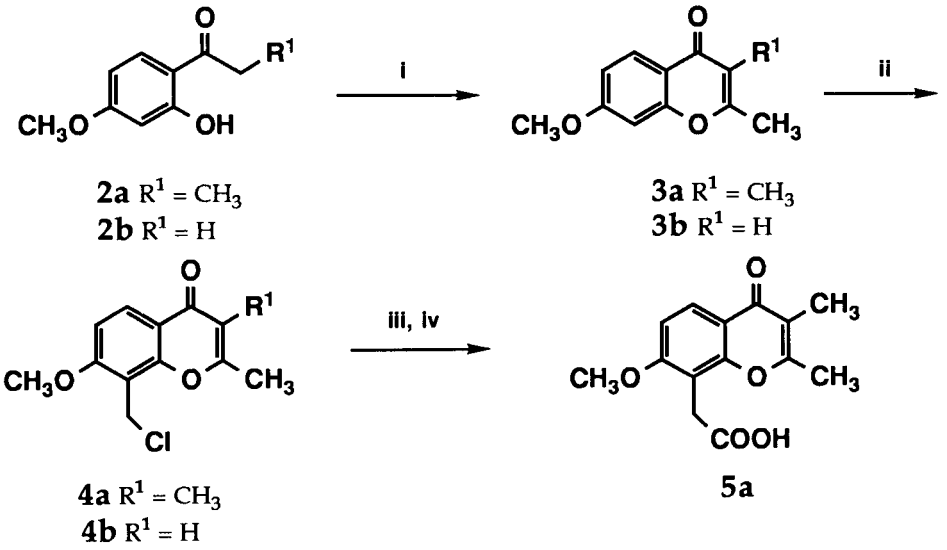
(2-Styrylchromon-8-yl)acetic acids, structural analogs of (flavon-8-yl)acetic acid (FAA) have been synthesized with satisfactory yields according to two different methods. The ^1H and ^{13}C nmr data fovor the *S-trans* stereoisomers.

J. Heterocyclic Chem., **28**, 2013 (1991).

Chromones or (4*H*-1-benzopyran-4-ones) are an important class of natural compounds [2]. Many pharmacological properties have been ascribed to various members of this family, including antiinflammatory, antiallergic and antitumor activities [3,4,5]. Elsewhere, we have described the preparation of 2-hydroxybenzoylalkylidene(triphenyl)-phosphoranes useful in the synthesis of 2-styrylchromones [6]. Here, we report further developments of this method in our research about structural analogs **1** of (flavon-8-yl)-acetic acid (FAA also called mitoflaxone) [7,8,9] with the goal of increasing *in vivo* activity. The most direct route to these compounds has been found by condensation of (2-methylchromon-8-yl)acetic acids with substituted benzaldehydes according to the following retrosynthetic scheme:



Scheme I (Route A)



2a $R^1 = CH_3$
2b $R^1 = H$

3a $R^1 = CH_3$
3b $R^1 = H$

4a $R^1 = CH_3$
4b $R^1 = H$

5a

i = a) $(CH_3CO)_2O$, CH_3COONa, b) Na_2CO_3 10% (for $R^1 = H$)(yield = 55%) ;
ii = $(CH_2O)_n$, HCl (yield = 87%) ;
iii = KCN, H_2O, C_2H_5OH (yield =70-75%) ; iv = CH_3COOH, H_2SO_4 (yield = 87%).

Using this strategy, the preparation of 2-methylchromones and the fixation of the acetic chain at the 8-position have been the key steps of the synthesis.

The 2-methylchromones had been obtained according to two methods (routes A and B) outlined in Schemes I and III. The choice of the method depends on the nature of the substituents R^1 and R^2.

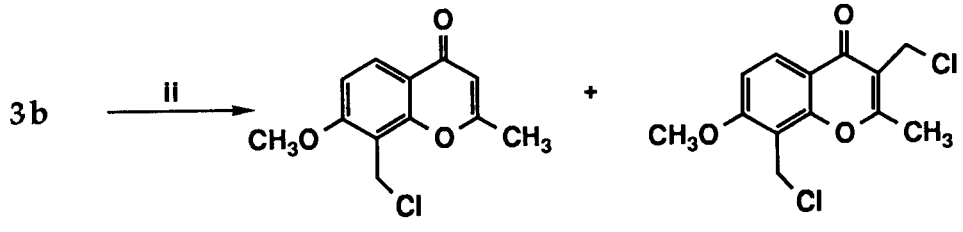
For $R^2 = OCH_3$, the first method uses 7-methoxy-2-methylchromones **3a,b** as starting materials, prepared according to the Kostanecki-Robinson procedure [2,10,11] by heating 4-methoxy-2-hydroxypropiophenone **2a** or 4-methoxy-2-hydroxyacetophenone **2b** with acetic anhydride. The compound **3a** treated with paraformaldehyde and hydrochloric acid afforded the chloromethyl derivative **4a** (Scheme I).

However, during the course of the Blanc reaction [12,13], the expected compound **4b** obtained in mixture with 3,8-bis-chloromethyl-2-methylchromone **6** was tediously separated by chromatographic methods or fractional crystallization (Scheme II).

(2-Methylchromon-8-yl)acetic acid **5a** is obtained as described for related compounds by reaction of potassium cyanide in ethanol, followed by acidic hydrolysis of nitrile.

The second method (Route B) uses 2,8-dimethylchromone **3c** as starting material. This compound is prepared by treating the benzoylmethylene(triphenyl)phosphorane **8** with acetic anhydride in toluene, according to a modification of the Le Corre's method [6,14]. The compound **3c** is regiospecifically brominated by *N*-bromosuccinimide and benzoyl peroxide under irradiation, leading to **9** [15].

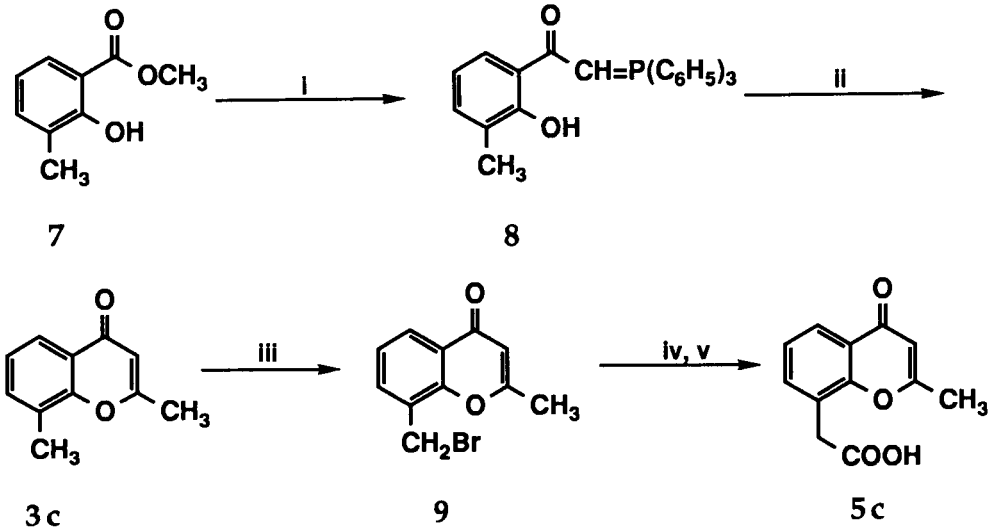
Scheme II



4b 35%

6 60%

Scheme III (Route B)



7 **8** **3c** **9** **5c**

i = $CH_2=P(C_6H_5)_3$, THF (yield = 70%) ;

ii = $(CH_3CO)_2O$, Pyridine (yield = 56%) ;

iii = NBS, $(C_6H_5CO)_2O_2$, CCl_4, hv (yield = 80%) ;

iv = $(C_2H_5)_4N^+CN^-$, CH_2Cl_2 (yield = 50%) ;

v = $(CH_3CO)_2O$, H_2SO_4 (yield = 96%)

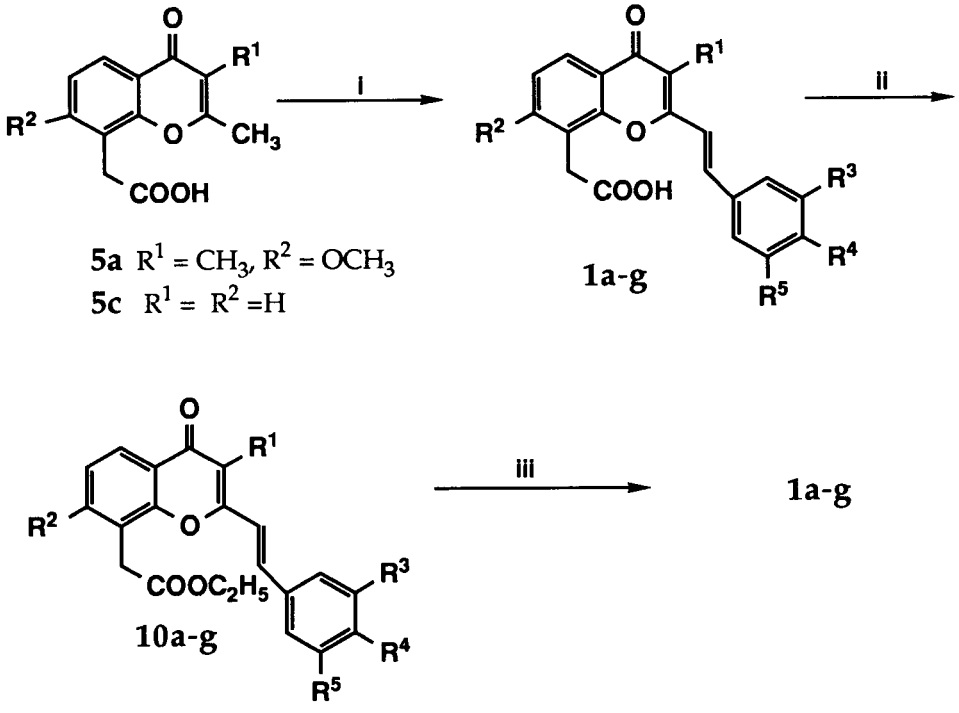
The following reactions to afford **5c** are classical: conversion of bromide **9** into nitrile according to a modified Simchen's procedure [16]. The average yield (about 50%) is far superior to that obtained following the potassium cyanide method (Scheme III).

For both routes, the last step of the synthesis consisted of the condensation of an aromatic aldehyde with 2-methylchromones **5a-c** under basic conditions (sodium methoxide) to afford the expected compounds **1a-g**.

However, depending on their degree of purity, these acids must be converted into ethyl esters **10**, easily purified by silica gel chromatography and then hydrolyzed in acidic medium (Scheme IV).

The structure of **1a-g** has been ascertained by standard methods. Characteristic infrared stretching bands were present at 1610-1635 cm^{-1} (ν C=O) and at 1710-1730 cm^{-1} (ν C=O acid). The ^{1}H-nmr spectra show a singlet at δ 6.40-6.50 ppm (**1a-c**) and a doublet at δ = 7.40 ppm ($^3J_{H-H}$ = 18 Hz) supporting the *E*-stereochemistry of the vinylic bond. The ^{13}C-nmr exhibits peaks at δ = 110 ppm (C_3), 170 ppm (C=O acid) and 180 ppm (C=O chromone). The NOESY experiments pointed out a *s-trans* conformation of the styryl group and this conformation is in good agreement with molecular design studies [17]. The fragmentation pattern of compounds **1a,d,e** in mass spectrometry is typical, with: (i) molecular peaks centered at m/z = 306

Scheme IV



i = (R^3, R^4, R^5)C_6H_2-CHO, CH_3ONa (4eq), CH_3OH (yield = 40-55%);
ii = C_2H_5OH, H_2SO_4 (yield = 90-95%); iii = CH_3COOH, HCl

1 or 10	R^1	R^2	R^3	R^4	R^5
a	H	H	H	H	H
b	H	H	OCH_3	OCH_3	OCH_3
c	H	H	H	COOH	H
d	CH_3	OCH_3	H	H	H
e	CH_3	OCH_3	OCH_3	OCH_3	OCH_3
f	CH_3	OCH_3	OCH_3	OCH_3	H
g	CH_3	OCH_3	H	COOH	H

Table 1. Physicochemical and Spectroscopic Data of (2-Styrylchromon-8-yl) acetic acids **1a-g**

Compound N°	Yield (%)	mp [a] °C	Molecular formula (mw) g	Analyses % Calcd.(Found) C	H	ir [b] cm^{-1}	^{1}H-nmr [c]	ms[d]
1a	55	202	$C_{19}H_{14}O_4$ (306.31)	74.50 (74.53)	4.61 4.60)	3200-2900, 1710, 1610	11.5(s,H,OH),8.0-7.3(m,10H), 6.45(s,1H,H^3), 4.0(s,2H,CH_2).	306(100),289 (85), 261(65), 128(70).
1b	62	212	$C_{22}H_{20}O_7$ (396.40)	66.66 (66.76)	5.08 (5.03)	3200-2500, 2820,1710, 1620	12.5(s,H,OH), 7.7-7.0(m,7H)- ,6.4(s,1H,H^3), 4.0 (s,2H,CH_2), 3.85(s,6H,$OCH_3$3',5'), 3.7(s,3H,-OCH_3-4').	/
1c	70	>305	$C_{20}H_{14}O_6$ (350.32)	68.57 (68.70)	4.03 (4.09)	3200-2500, 1730,1710, 1620	13.0(s,H,OH), 8.0-7.2(m,10H), 6.5(s,1H,H^3),4.0(s,2H,CH_2).	/
1d	32	254	$C_{21}H_{18}O_5$ (350.37)	71.99 (71.86)	5.18 (5.15)	3600-3200, 1720, 1630	12.0(s,H,OH), 8.0-7.2(m,9H), 3.95(s,3H,OCH_3), 3.90 (s,2H, CH_2), 2.15(s,3H,CH_3).	350(100),349 (95),273(90), 335(50), 141 (25).
1e	42	240	$C_{24}H_{24}O_8$ (440.45)	65.45 (65.35)	5.49 (5.39)	3600-3200 1720,1630	12.0(s,H,OH), 7.5-7.0(m,6H), 3.95(s,9H, OCH_3), 3.85(s,3H, OCH_3), 3.90 (s,2H,CH_2), 2.15(s,3H,CH_3).	440(100),439 (90), 425(50), 395(15), 231 (25).
1f	40	245	$C_{23}H_{22}O_7$ (410.45)	67.30 (67.27)	5.40 (5.35)	3600-3200, 1710, 1610	12.0(s,H,OH), 7.95(d,1H,J=9), 7.5-7.0(m,4H), 7.30(d,1H,J=18), 7.05-(d, 1H,J=18),3.95(s,6H, OCH_3), 3.85(s,3H,OCH_3), 3.90 (s,2H,CH_2),2.15(s,3H,CH_3)	/
1g	40	>305	$C_{22}H_{18}O_7$ (394,31)	67.00 (67.06)	4.60 (4.61)	3600-3100 1730,1710, 1620	12.0(s,H,OH), 8.5-7.8(m,6H), 7.50(AA'BB', 2H,Har), 7.20(d, 1H,J=9),3.95(s,3H,OCH_3), 3.90 (s,2H, CH_2), 2.15 (s,3H,CH_3).	/

[a] crystallized from ethanol. [b] realized in potassium bromide. [c] δ (ppm) from tetramethylsilane. [d] (70 eV) m/z (%)

(**1a**), 350 (**1d**), 440 (**1e**) (M^+); (ii) peaks at m/z = 349, 335 (**1a**) and 439,425 (**1e**) issued from the loss of an hydrogen ion and a methyl group respectively; and (iii) peaks at m/z = 128 ($C_{10}H_8^+$, **1a**), 141 ($C_{11}H_9^+$, **1d**), 231 ($C_{14}H_{15}O_3^+$, **1e**) due to cleavage of chromone ring (Table 1).

In conclusion, the synthesis of (2-styrylchromon-8-yl)acetic acids proves the value of the acylphosphorane route. This method allows us to depart from the Kostanecki-Robinson reaction, inconsistent with the synthesis of non-substituted chromones and generally giving low yields and to use more readily available salicylic acid derivatives.

EXPERIMENTAL

Melting points were determined on a Kofler 7841 melting point apparatus and are uncorrected. The ^{1}H-nmr and ^{13}C-nmr spectra were measured on a Bruker AC 100 using tetramethylsilane as an internal reference. Mass spectra were recorded on a Varian-MAT-112 mass spectrometer. IR spectra were obtained using a Beckman ir-4230. Thin layer chromatography used Merck silica gel plates of type 60 F_{254} and 0.25 mm layer thickness. The 2,4-dihydroxyacetophenone and -propiophenone were purchased from Janssen and Lancaster. Compounds **2a** and **2b** were prepared from 2,4-dihydroxypropiophenone and 2,4-dihydroxyacetophenone respectively, by reaction with methyl iodide in presence of the couple potassium carbonate/acetone. Compounds **3a**, **3b** and **7** were obtained in essentially the same way as reported in literature [18,19,20].

(2-Styrylchromon-8-yl)acetic Acids **1a-g**. Typical Procedure.

To a solution of (2-methylchromon-8-yl)acetic acid **5** (3.34 mmoles) and the appropriate aromatic aldehyde (3.4 mmoles) in 200 ml of anhydrous methanol was added an alcoholic sodium methylate (6.7 mmoles) solution from sodium (0.155 g) in anhydrous methanol (20 ml), and the reaction mixture was refluxed for a period ranging from 7 hours to 24 hours. The solvent was then removed under vacuum and the crude residue was dissolved in a hot 5% sodium hydrogenocarbonate solution and filtered. After cooling, the filtrate was acidified with *N* hydrochloric acid and the formed precipitate filtered off and washed with water; crystallization from ethanol gave the title compounds **1** (Table 1).

2,8-Dimethylchromone (**3c**).

(2-Hydroxy-3-methylbenzoyl)methylene(triphenyl)phosphorane **8** (40 g, 97 mmoles) was dissolved in boiling dry toluene (250 ml); acetic anhydride (19 ml, 190 mmoles) and pyridine (17 ml, 210 mmoles) were added. The mixture was refluxed for 5 hours and then allowed to cool. The pyridinium salt was separated by filtration. The filtrate was washed with aqueous 15% sodium carbonate solution and the toluene distilled off. The solid residue was purified by chromatography on silica gel column (70-230 mesh) using methylene chloride/methanol (99:1) as eluent. Pure **3c** was first eluted; 9.5 g (56% yield), mp 114°; ^{1}H-nmr (deuteriochloroform): δ = 8.00 (dd, 1H, H^5, J = 8 Hz, J = 2 Hz), 7.50 (dd, 1H, H^7, J = 8 Hz, J = 2 Hz), 7.25 (t, 1H, H^6, J = 8 Hz), 6.20 (s, 1H, H^3), 2.50 (s, 3H, $CH_{3\text{-}2}$), 2.40 (s, 3H, $CH_{3\text{-}8}$); ir (potassium bromide): 1640 (C=O), 1600 (C=C) cm^{-1}.

Anal. Calcd. for $C_{11}H_{10}O_2$: C, 75.84; H, 5.78. Found: C, 75.90; H, 5.75.

8-Chloromethyl-7-methoxy-2,3-dimethylchromone (**4a**).

A mixture of **3a** (4.9 g, 23.48 mmoles), concentrated hydrochloric acid (35 ml) and polyoxymethylene (40 mmoles) was stirred at 70° for 7 hours. The reaction mixture was then poured into ice-water (100 ml) and left to stand overnight. The separated solid was filtered, washed with water and dried. The crude product **4a**, after crystallization from cyclohexane, gave a white crystalline solid; 5.15 g (87% yield), mp 171°; ^{1}H-nmr (deuteriochloroform): δ = 8.20 (d, 1H, H^5, J = 9 Hz), 7.00 (d, 1H, H^6, J = 9 Hz), 4.90 (s, 2H, CH_2Cl), 4.00 (s, 3H, OCH_3), 2.45 (s, 3H, $CH_{3\text{-}2}$), 2.05 (s, 3H, $CH_{3\text{-}3}$); ir (potassium bromide): 1640 (C=O), 1600 (C=C), 790 (C-Cl) cm^{-1}.

Anal. Calcd. for $C_{13}H_{13}O_3Cl$: C, 61.57; H, 5.17; Cl, 13.98. Found: C, 61.60; H, 5.15; Cl, 13.97.

8-Chloromethyl-7-methoxy-2-methylchromone (**4b**).

A mixture of **3b** (26 g, 137 mmoles), acetic acid (270 ml), concentrated hydrochloric acid (200 ml) and formalin 37% (75 ml) was stirred at 70° for 7 hours, meanwhile a stream of hydrogen chloride was introduced. The reaction mixture was then poured into ice-water (400 ml) and left to stand overnight. The separated solid was filtered, washed with water and dried. The crude product was purified by chromatography on silica gel column (70-230 mesh) using methylene chloride/methanol (99:1) as eluent. Pure **6** was first isolated as white crystals and next **4b** as yellow crystals: (35% yield), mp 146°; ^{1}H-nmr (deuteriochloroform): δ = 8.20 (d, 1H, H^5, J = 9 Hz), 7.00 (d, 1H, H^6, J = 9 Hz), 6.15 (s, 1H, H^3), 4.90 (s, 2H, CH_2Cl), 4.00 (s, 3H, OCH_3), 2.40 (s, 3H, CH_3); ir (potassium bromide): 2820 (OCH_3), 1660 (C=O), 790 (C-Cl) cm^{-1}.

Anal. Calcd. for $C_{12}H_{11}O_3Cl$: C, 60.50; H, 4.65; Cl, 14.88. Found: C, 60.23; H, 4.63; Cl, 14.87.

3,8-Bis-chloromethyl-2-methylchromone (**6**).

Compound **6** was obtained in 60% yield, mp 206°; ^{1}H -nmr (deuteriochloroform): δ = 8.20 (d, 1H, H^5, J = 9 Hz), 7.00 (d, 1H, H^6, J = 9 Hz), 4.90 (s, 2H, $CH_2Cl_{\text{-}8}$), 4.60 (s, 2H, $CH_2Cl_{\text{-}3}$), 4.00 (s, 3H, OCH_3), 2.60 (s, 3H, CH_3); ir (potassium bromide): 2820 (OCH_3), 1660 (C=O), 790 (C-Cl) cm^{-1}.

Anal. Calcd. for $C_{13}H_{12}O_3Cl_2$: C, 54.55; H, 4.22; Cl, 24.72. Found: C, 54.60; H, 4.18; Cl, 24.77.

(7-Methoxy-2,3-dimethylchromon-8-yl)acetic Acid (**5a**).

Potassium cyanide (1.47 g, 22.53 mmoles) was dissolved in water (8 ml) and heated to 60-70°. A suspension of **4a** (3.27 g, 12.96 mmoles) in 38 ml boiling ethanol was added portionwise. The mixture was stirred under reflux for 4 hours, filtered hot and kept overnight in a refrigerator. The precipitate was filtered off and purified by chromatography on silica gel column (70-230 mesh) using methylene chloride as eluent to afford the corresponding acetonitrile derivative as white crystals 2.45 g (77% yield), mp 185°; ^{1}H-nmr (deuteriochloroform): δ = 8.15 (d, 1H, H^5, J = 9 Hz), 7.00 (d, 1H, H^6, J = 9 Hz), 4.00 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2CN), 2.45 (s, 3H, $CH_{3\text{-}2}$), 2.05 (s, 3H, $CH_{3\text{-}3}$); ir (potassium bromide): 2820 (OCH_3), 2220 (CN), 1640 (C=O) cm^{-1}.

To a mixture of this corresponding 8-cyanomethyl-2-methylchromone (0.70 g, 2.87 mmoles), acetic acid (4 ml) and water (4 ml) under stirring, was added for 4 hours. After cooling, the reaction mixture was poured into ice-water (250 ml) and kept overnight at 5°. The precipitate was filtered off, dissolved in warm 5% sodium hydrogenocarbonate solution (50-60°). After filtration, the cooled solution was acidified with concentrated hydro-

chloric acid. The precipitate was filtered off, thoroughly washed with water, dried and crystallized from ethanol to give 0.65 g (87% yield) of **5a** as pale yellow crystals, mp 211°; ^{1}H-nmr (DMSO-d_6): δ = 12.60 (s, 1H, OH), 7.95 (d, 1H, H^5, J = 9 Hz), 7.20 (d, 1H, H^6, J = 9 Hz), 3.90 (s, 3H, OCH_3), 3.70 (s, 2H, CH_2COOH), 2.40 (s, 3H, $CH_{3\text{-}2}$), 1.90 (s, 3H, $CH_{3\text{-}3}$); ir (potassium bromide): 3300-3200 (OH), 2820 (OCH_3), 1740 (C=O acid), 1630 (C=O) cm^{-1}.

Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.05; H, 5.33.

(2-Methylchromon-8-yl)acetic Acid (**5c**).

To a solution of **9** (5.9 g, 23 mmoles) in 200 ml of anhydrous methylene chloride, was added tetraethylammonium cyanide (5.45 g, 35 mmoles), and the reaction mixture was stirred overnight at room temperature. The solvent was evaporated *in vacuo* and the residue treated with water, extracted with methylene chloride. The organic phase was dried and evaporated. The residual product was purified by chromatography on silica gel column (70-230 mesh) using methylene chloride as eluent to give 2.40 g (52% yield) of 8-cyanomethyl-2-methylchromone as white crystals, mp 138°; ^{1}H-nmr (deuteriochloroform): δ = 8.20 (dd, 1H, H^5, J = 9 Hz, J = 2 Hz), 7.80 (dd, 1H, H^7, J = 9 Hz, J = 2 Hz), 7.50 (t, 1H, H^6, J = 9 Hz), 6.20 (s, 1H, H^3), 3.95 (s, 2H, CH_2CN), 2.45 (s, 3H, $CH_{3\text{-}2}$); ir (potassium bromide): 2220 (CN), 1640 (C=O), 1600 (C=C) cm^{-1}.

To a mixture of the 8-cyanomethyl-2-methylchromone (0.70 g, 3.5 mmoles), acetic acid (4 ml) and water (4 ml) under stirring, was added slowly concentrated sulfuric acid (4 ml). Reflux was then maintained for 4 hours. After cooling, the reaction mixture was poured into ice-water (250 ml) and kept overnight at 5°. The precipitate was filtered off, dissolved in warm 5% sodium hydrogenocarbonate solution (50-60°). After filtration the cooled solution was acidified with concentrated hydrochloric acid. The precipitate was filtered off, thoroughly washed with water, dried and crystallized from ethanol to give 0.73 g (96% yield) of **5c** as pale yellow crystals, mp 228°; ^{1}H-nmr (DMSO-d_6): δ = 12.50 (s, 1H, OH), 8.00 (dd, 1H, H^5, J = 9 Hz, J = 2 Hz), 7.60 (dd, 1H, H^7, J = 9 Hz, J = 2 Hz), 7.40 (t, 1H, H^6, J = 9 Hz), 6.25 (s, 1H, H^3), 3.90 (s, 2H, CH_2COOH), 2.35 (s, 3H, $CH_{3\text{-}2}$); ir (potassium bromide): 3400-3200 (OH), 1700 (C=O acid), 1640 (C=O) cm^{-1}.

Anal. Calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 66.15; H, 4.53.

(2-Hydroxy-3-methylbenzoyl)methylene(triphenyl)phosphorane (**8**).

To a stirred slurry of methylene(triphenyl)phosphorane (prepared from methyltriphenylphosphonium iodide (14.6 g, 36 mmoles) and 1.6*M* butyllithium in hexane (31.25 ml, 50 mmoles) in anhydrous tetrahydrofuran (120 ml) under nitrogen with stirring at room temperature for 3 hours) a solution of methyl 3-methyl-2-hydroxybenzoate **7** (3 g, 18 mmoles) in anhydrous tetrahydrofuran (20 ml) was slowly added. The resulting mixture was kept at 60° for 3 hours. Lithium iodide was then filtered off at room temperature and the solvent evaporated. From the crude residue, the phosphorane was recovered by crystallization in methanol to give 4.8 g (65% yield), mp 170°; ^{1}H nmr (deuteriochloroform): δ = 7.80-7.35 (m, 17H), 7.15 (d, 1H, H^4, J = 7 Hz), 6.90 (d, 1H, $^2J_{H\text{-}P}$ = 37 Hz), 6.65 (t, 1H, H^5, J = 7 Hz), 2.20 (s, 3H); ir (potassium bromide): 3200-3100 (OH), 1590 (C=O) cm^{-1}.

Anal. Calcd. for $C_{27}H_{23}O_2P$: C, 79.01; H, 5.65. Found: C, 79.02; H, 5.61.

8-Bromomethyl-2-methylchromone (**9**).

To a suspension of **3c** (3 g, 17 mmoles) in carbon tetrachloride (50 ml) was added *N*-bromosuccinimide (3.5 g, 20 mmoles) and benzoyl peroxide (1.5 mg). The reaction mixture was refluxed for 6 hours under irradiation (Philips lamp DE/500 W), and filtered hot to remove the resultant succinimide. Removal of the solvent gave a gummy product which was crystallized from cyclohexane to give 3.45 g (80% yield) of **9**, mp 100°; ^{1}H-nmr (deuteriochloroform): δ = 8.20 (dd, 1H, H^5, J = 7 Hz, J = 2 Hz), 7.95 (dd, 1H, H^7, J = 7 Hz, J = 2 Hz), 7.30 (t, 1H, H^6, J = 7 Hz), 6.20 (s, 1H, H^3), 4.70 (s, 2H, CH_2Br), 2.45 (s, 3H, $CH_{3\text{-}2}$); ir (potassium bromide): 1640 (C=O), 1600 (C=C), 790 (C-Br) cm^{-1}.

Anal. Calcd. for $C_{11}H_9O_2Br$: C, 52.20; H, 3.58; Br, 31.57. Found: C, 52.23; H, 3.63; Br, 31.58.

Ethyl (2-Styrylchromon-8-yl)acetate (**10d-f**): Typical Procedure.

A mixture of **1** (1.80 mmoles), 60 ml of anhydrous ethanol and 1.5 ml of concentrated sulfuric acid was refluxed for 7 hours, then cooled overnight at 0-4°. The precipitate was filtered off and purified by chromatography on silica gel column (70-230 mesh) using methylene chloride/methanol (98:2) as eluent to afford **10** as pure yellow crystals.

Ethyl (7-Methoxy-3-methyl-2-styrylchromon-8-yl)acetate (**10d**).

Compound **10d** was obtained in 98% yield; ^{1}H-nmr (DMSO-d_6): δ = 8.15 (d, 1H, H^5, J = 9 Hz), 7.65-7.20 (m, 7H, Har', Hvinyl), 7.00 (d, 1H, H^6, J = 9 Hz), 4.20 (q, 2H, J = 7 Hz, $COOCH_2$-CH_3), 4.00 (s, 3H, OCH_3), 3.95 (s, 2H, CH_2COOEt), 2.25 (s, 3H, $CH_{3\text{-}3}$), 1.20 (t, 3H, J = 7 Hz, CH_2-CH_3); ir (potassium bromide): 2820 (OCH_3), 1730 (C=O ester), 1630 (C=O) cm^{-1}.

Ethyl [7-Methoxy-3-methyl-2-[2-(3,4,5-trimethoxyphenyl)vinyl]-chromon-8-yl]acetate (**10e**).

Compound **10e** was obtained in 98% yield; ^{1}H-nmr (DMSO-d_6): δ = 8.00 (d, 1H, H^5, J = 9 Hz), 7.40-6.85 (m, 4H, Har, Hvinyl), 6.95 (d, 1H, Hvinyl, J = 18 Hz), 4.05 (q, 2H, J = 7 Hz, $COOCH_2$-CH_3), 3.95 and 3.90 (s, 12H, OCH_3), 3.85 (s, 2H, CH_2COOEt), 2.15 (s, 3H, $CH_{3\text{-}3}$), 1.15 (t, 3H, J = 7 Hz, CH_2-CH_3); ir (potassium bromide): 2820 (OCH_3), 1725 (C=O ester), 1610 (C=O) cm^{-1}.

Ethyl [7-Methoxy-3-methyl-2-[2-(3,4-dimethoxyphenyl)vinyl]chromon-8-yl]acetate (**10f**).

Compound **10f** was obtained in 98% yield; ^{1}H-nmr (DMSO-d_6): δ = 7.95 (d, 1H, H^5, J = 9 Hz), 7.40-7.05 (m, 6H, Har, Hvinyl), 4.15 (q, 2H, J = 7 Hz, $COOCH_2$-CH_3), 3.95 and 3.90 (s, 9H, OCH_3), 3.70 (s, 2H, CH_2COOEt), 2.20 (s, 3H, $CH_{3\text{-}3}$), 1.15 (t, 3H, J = 7 Hz, CH_2-CH_3); ir (potassium bromide): 2820 (OCH_3), 1735 (C=O ester), 1610 (C=O) cm^{-1}.

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